IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVARTIS PHARMACEUTICALS CORPORATION, NOVARTIS AG, NOVARTIS PHARMA AG, NOVARTIS INTERNATIONAL PHARMACEUTICAL LTD. and LTS LOHMANN THERAPIE-SYSTEMEAG,	)	
Plaintiffs,	)	C. A. Nos. 13-00527 & 14-111 (RGA)
	)	(Consolidated)
v.	)	
NOVEN PHARMACEUTICALS, INC.,	)	
Defendant.	)	

NOVEN'S OPENING POST TRIAL BRIEF ON INVALIDITY

PHILLIPS, GOLDMAN & SPENCE, P.A.
John C. Phillips, Jr. (No. 110)
Megan C. Haney (No. 5016)
1200 North Broom Street
Wilmington, DE 19806
(302) 655-4200
jcp@pgslaw.com
mch@pgslaw.com

Attorneys for Defendant
Noven Pharmaceuticals, Inc.

KENYON & KENYON LLP
Steven J. Lee (*pro hac vice*)
Michael K. Levy (*pro hac vice*)
Christopher J. Coulson (*pro hac vice*)
One Broadway
New York, NY 10004-1007
(212) 425-7200

Of Counsel

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I. STATEMENT OF NATURE AND STAGE OF PROCEEDING

Defendant Noven Pharmaceuticals, Inc. ("Noven") respectfully submits this Post-Trial Brief pursuant to the Court's Joint Stipulation and Order Regarding Post-Trial Briefing, D.I. 152.[1] The only issue before the Court is the validity of claims 7 and 16 of U.S. Patent No. 6,335,031 (JTX 1, the "'031 patent") asserted by Novartis Pharmaceuticals Corporation, Novartis AG, Novartis Pharma AG and Novartis International Pharmaceutical Ltd. and LTS Lohmann Therapie-Systeme AG ("LTS") (together with Novartis, "Plaintiffs"). The Court held a two-day bench trial on December 1-2, 2014, and received testimony from Noven's experts Drs. Schöneich and Kydonieus, and Plaintiffs' expert Dr. Klibanov.

II. SUMMARY OF ARGUMENT

The Court previously heard evidence regarding, among other things, the validity of claims 7 and 16 of the '031 patent in the Watson litigation, and concluded that "the obviousness determination in this case turns on whether a PHOSITA in January 1998, looking at all of the prior art, would have known rivastigmine was susceptible to oxidative degradation. If the answer is yes, the asserted claims of the '023 and '031 patents are invalid because the addition of an antioxidant to a pharmaceutical composition that oxidatively degrades is one of several known, obvious solutions." Trial Opinion, *Novartis Pharms. Corp. v. Watson Labs., Inc.*, C.A. 11-1112, D.I. 40 at 40 (D. Del. June 18, 2014). In the present case, Noven has proven by clear and convincing evidence, unrebutted on its scientific basis, that a person of ordinary skill in the art in January 1998 ("POSA")[2] would have indeed maintained a reasonable expectation that rivastigmine was susceptible to oxidative degradation. Combined with the prior art's undisputed disclosure of transdermal devices containing rivastigmine and the use of antioxidants to prevent

[1] All docket citations refer to C.A. No. 13-527 unless otherwise noted.

[2] "POSA" refers to a person of ordinary skill in the art as of January 12, 1998.

oxidative degradation issues in pharmaceutical formulations, including transdermals, Noven has proved, by clear and convincing evidence, that claims 7 and 16 of the '031 patent are invalid for obviousness.[3]

III. STATEMENT OF FACT

In accordance with the Court's Order, Noven's Statement of Facts is separately presented and submitted herewith, cited as SOF ("Statement of Facts"). (*See* C.A. 13-cv-527, D.I. 153.)

IV. LEGAL PRINCIPLES

Section 103(a) of the patent statute forbids issuance of a patent when the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 406 (2007) (internal quotations omitted); *see* pre-AIA 35 U.S.C. § 103(a). Obviousness is a question of law based on underlying factual determinations, including the scope and content of the prior art; the level of ordinary skill in the art; and the differences between the claimed invention and the prior art. *L-3 Commc'ns. Corp v. Sony Corp.*, No. 10-734-RGA, 2014 US Dist. LEXIS 127643 at *8-9 (D. Del. Sept. 12, 2014) (holding patent obvious based on a combination of prior art references) (memorandum opinion).

Motivation to combine known elements in the prior art to achieve the claimed invention "can come from the prior art, the background knowledge of one of ordinary skill in the art, the nature of any problem or need to be addressed, market demand, or common sense." *Id.* at *9-10, *citing KSR*. The motivation to combine references need not be explicitly stated in the prior art—expert testimony explaining the knowledge of one or ordinary skill in the art is enough. *Alza*

[3] The parties agreed to present no evidence of "secondary considerations." (C.A. No. 13-537, D.I. 154 at 131:10-13.)

Corp. v. Mylan Labs., Inc., 464 F.3d 1286, 1294 (Fed. Cir. 2006) (motivation to combine can be found in the general knowledge available to a POSA); *see Allergan, Inc. v. Sandoz, Inc.*, 726 F.3d 1286, 1292 (Fed. Cir. 2013) (motivation to combine references can be found "in many different places and forms.") The Supreme Court has stated that "if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond" his or her skill. *KSR* at 417.

New evidence that was not considered by the PTO may carry more weight than evidence previously considered by the PTO, making it easier for the patent challenger to carry its burden of proof. *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2241 (2011) ("Simply put, if the PTO did not have all material facts before it, its considered judgment may lose significant force. And, concomitantly, the challenger's burden to persuade the jury of its invalidity defense by clear and convincing evidence may be easier to sustain.") (citation omitted); *Sciele Pharma Inc. v. Lupin Ltd.*, 684 F.3d 1253, 1260 (Fed. Cir. 2012).

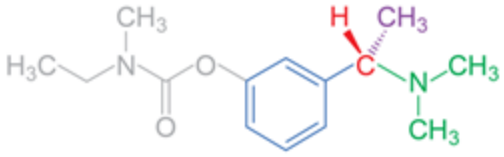
V. ARGUMENT

A. A POSA Would Have Known That Rivastgimine Was Susceptible to Oxidative Degradation

A POSA would have been motivated to add an antioxidant to compositions containing rivastigmine because she would have recognized that rivastigmine was inherently susceptible to oxidative degradation. An analysis of rivastigmine's chemical structure would have been part of routine formulation work, and would have identified features rendering the molecule inherently susceptible to oxidation. The POSA's expectation that rivastigmine was inherently susceptible to oxidative degradation would have been further reinforced by the relevant structural similarities between rivastigmine and nicotine, a compound having known susceptibility to oxidation.

1. A POSA Would Have Recognized that Rivastigmine Was Inherently Susceptible to Oxidative Degradation Based on its Chemical Structure.

A POSA would have examined the structure of rivastigmine as a routine part of formulation development in order to evaluate possible degradation issues.[4] (SOF 157.) Prior art confirms that, analysis of pharmaceutical stability is "one of the most important activities of pre-formulation work," and that "[i]nitial investigation begins through knowledge of the drug's chemical structure which allows the preformulation scientist to anticipate the possible degradation reactions." (SOF 106, 157.) A POSA knowledgeable in organic chemistry would have known that weak bonds in a molecule were susceptible to free-radical reactions, including oxidation; and upon examination of rivastigmine's structure, it would have been immediately apparent to that POSA that rivastigmine has a particularly weak carbon-hydrogen bond. (SOF 142, 145, 158-60.) As Dr. Schöneich explained, a POSA would have recognized that rivastigmine has three structural features that create an "electronic neighborhood" that renders a specific carbon-hydrogen bond in the molecule "particularly susceptible" to oxidation: the carbon-hydrogen bond (in red below) is *immediately adjacent* to each of (i) an aromatic ring (in blue below); (ii) a tertiary amine (in green below); and (iii) an additional carbon substituent (–CH_3, in purple below), making the carbon a tertiary carbon. (SOF 158-60.)



[4] There is no dispute that a POSA could be a collaborative team which had knowledge of organic chemistry or consulted with a collaborator with knowledge of organic chemistry. (SOF 1-2.)

Dr. Schöneich explained how each of these features was known to reduce the bond strength of an adjacent carbon-hydrogen bond thereby making that bond more susceptible to abstraction of the hydrogen atom and hence radical formation. (SOF 143-45, 159.) Dr. Schöneich explained how tertiary carbon-hydrogen bonds are weaker than hydrogen bonds to primary or secondary carbons because the resulting radical at the tertiary carbon is more stable. (SOF 146 at Tr. 59:24-60:21.)[5] Dr. Schöneich also explained how a tertiary amine reduces the carbon-hydrogen bond strength at an adjacent carbon (SOF 147), and that an adjacent aromatic ring reduces the carbon-hydrogen bond strength at the adjacent carbon by stabilizing the radical at that carbon through electron delocalization (SOF 148). He further demonstrated that the effects of neighboring atoms and structures were well characterized because the bond dissociation energies for different structural motifs are cataloged in organic chemistry textbooks including the carbon-hydrogen bond dissociation energies for primary, secondary and tertiary carbons, and benzylic carbon (a carbon adjacent to an aromatic benzene ring). (SOF 146, 150.) Dr. Schöneich explained that each of these structural features by themselves were known to reduce the carbon-hydrogen bond strength at an adjacent carbon, but that the presence of *all three* in rivastigmine would have alerted a POSA that the subject carbon-hydrogen bond was particularly susceptible to oxidation. (SOF 158-60.) Plaintiffs' expert, Dr. Klibanov, agreed that rivastigmine has these three structural features (a carbon-hydrogen bond at a tertiary carbon that is immediately adjacent to both an aromatic ring and a tertiary amine) (Tr. 538:17-542:17; 543:5-11) and he never disputed that these features would cause the subject carbon-hydrogen bond to be particularly weak, and the rivastigmine molecule therefore susceptible to radical formation.

[5] Citations to "Tr." are to D.I. 154-56 in C.A. No. 13-537.

In fact, Dr. Klibanov intentionally avoided addressing the scientific basis for Dr. Schöneich's testimony. (Tr. 316:18-317:1; 436:5-20.)

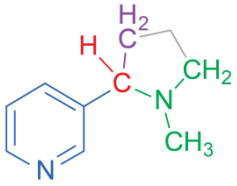
The presence of a weak carbon-hydrogen bond was known to cause a drug molecule to be susceptible to oxidative degradation. (SOF 145.) As Dr. Schöneich explained, when an initiator of oxidation is present in a formulation, the initiator can break this weak bond to hydrogen—abstracting the hydrogen—and leaving a carbon radical on the drug molecule. (SOF 136-37.) Due to the presence of the radical on the drug, the drug will be highly reactive, and will react with oxygen to form reactive peroxides, and can react with other constituents in the formulation leading to destruction of the drug. (SOF 139-40.) The reactive radicals can even react with additional drug molecules causing a chain reaction that can lead to significant degradation of the drug over time. (SOF 140.) Dr. Schöneich's testimony that these reactions were known to occur in pharmaceutically-relevant time frames, (SOF 141), was not disputed.

2. The Similarity Between Rivastigmine and Nicotine Would Have Reinforced the POSA's Expectation that Rivastigmine Was Susceptible to Oxidative Degradation.

The structural similarity of rivastigmine to nicotine, coupled with nicotine's known susceptibility to oxidative degradation, would have reinforced the POSA's reasonable expectation that rivastigmine would be susceptible to oxidation. Chemists of ordinary skill in the art understand that compounds with similar structures often have similar properties. *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 752 F.3d 967, 976 (Fed. Cir. 2014) ("it is well settled that structurally similar compounds often have similar properties"); *see Aventis Pharma. Deutschland GmbH v. Lupin, Ltd.*, 499 F.3d 1293, 1301 (Fed. Cir. 2007) (referring to a presumed expectation that structurally similar compounds have similar properties) (citation omitted).

There was no dispute among the experts that nicotine was known to be susceptible to oxidation. (SOF 162.) Dr. Schöneich cited authority from 1960 that determined that nicotine was susceptible to oxidation at the corresponding carbon-hydrogen bond and that this oxidation could be prevented by the addition of an antioxidant, BHT. (SOF 112-14.) Dr. Klibanov testified that as of 1998, nicotine was known to undergo oxidative degradation under pharmaceutically relevant conditions (SOF 162 at Tr. 452:1-5), and stated that Habitrol, a marketed nicotine transdermal patch, utilized an airtight packaging to exclude oxygen and prevent oxidation of nicotine. (SOF 164.) Dr. Kydonieus discussed JTX 28 (Ebert), which states "[a]nother trait of nicotine that can be problematic is its tendency to oxidize readily in the presence of light and air." (SOF 67.)

The POSA would have recognized that nicotine contains the same three structural features that render rivastigmine particularly susceptible to oxidative degradation. Dr. Klibanov agreed with Dr. Schöneich that both have a carbon-hydrogen bond at a carbon that is (i) a tertiary carbon (in red below), and is (ii) immediately adjacent to an aromatic ring (in blue below) and (iii) immediately adjacent to a tertiary amine (in green below). (SOF 161.)



While Dr. Klibanov points out nominal differences between the structures of the two molecules (Tr. 448:19-451:15) (differences already acknowledged by Dr. Schöneich (Tr. 88:12-89:1-10; 104:17-105:2)), Dr. Klibanov did not provide any reason that such differences would prevent a POSA from drawing conclusions based on the similarities in structure. For example, both Dr. Klibanov and Dr. Schöneich testified that the aromatic ring in nicotine has a nitrogen (and is thus a pyridine ring) whereas the aromatic ring in rivastigmine is a benzene ring and does not contain

a nitrogen. (Tr. 88:12-17; 451:5-8.) This distinction, however, is without difference because both aromatic rings have the same effect on the adjacent carbon-hydrogen bond, namely, making the carbon-hydrogen bond weaker by resonance stabilization (delocalization) of a radical at the carbon. (SOF 163.) Dr. Klibanov admitted that the aromatic ring in nicotine will stabilize a radical at the adjacent carbon by resonance (unless the nicotine is in an acidic aqueous solution—a qualification irrelevant to the comparison of the two drugs). (Tr. 542:1017; 543:5-11.) The structural similarities between nicotine and rivastigmine, and nicotine's known susceptibility to oxidative degradation, would have reinforced the POSA's expectation that rivastigmine would also be susceptible to oxidative degradation. (SOF 165.)

3. Once the Susceptibility to Oxidative Degradation Was Recognized, a POSA Would Have Taken Steps to Address the Issue, Including Adding an Antioxidant.

Once a POSA recognized during the preformulation examination of the drug's structure that rivastigmine was inherently susceptible to oxidation, he or she would have taken steps to address this susceptibility. (SOF 105-6, 134.) Dr. Schöneich explained that a POSA would have set up a matrix of test formulations and would have included a selection of antioxidants in the test formulations. (SOF 134.) Dr. Kydonieus confirmed that when a drug was identified as susceptible to oxidation, it was routine to address this issue early in the development process by including antioxidants in test formulations. (SOF 134 at Tr. 147:3-148:10.)

4. Plaintiffs' Rebuttal of Dr. Schöneich's Testimony Fails.

Dr. Klibanov explicitly elected to ignore the scientific basis of Dr. Schöneich's testimony in favor of challenging it in a less direct manner. (Tr. 316:18-317:1; *see also* 436:5-20.) While overtly avoiding the scientific basis for Dr. Schöneich's testimony that the POSA would reasonably expect rivastigmine to be susceptible to oxidative degradation, Plaintiffs' disparate rebuttal evidence is either contradicted by their own expert or irrelevant.

(a) Susceptibility to Oxidation Was Predictable.

Dr. Klibanov's testimony that "a POSA could not reasonably and correctly predict the oxidative instability of a compound merely based on the structure" (Tr. 323:23-324:3) is inconsistent with both his own testimony and the exhibits upon which he relies. Dr. Klibanov cites to no authority stating that a POSA cannot reasonably predict a compound's susceptibility to oxidation. To the contrary, Dr. Klibanov testified from *Modern Pharmaceutics* (PTX 153), which he acknowledged is an authoritative text in pharmaceutics, (Tr. 523:24-524:2), and agreed with the statement from this text that by looking at functional groups in a molecule's chemical structure, "it is possible to anticipate the potential modes of degradation that drug molecules will likely undergo:"

> Q. It says, "Yet through the application of functional group chemistry, it is possible to anticipate the potential modes of degradation that drug molecules will likely undergo." Do you agree with it?
>
> A. I do. And in particular, I want to again emphasize the word potential, which is found in this sentence. With the word potential there, I do agree with this sentence. Yes, sir.

(Tr. 528:23-529:8 (emphasis added)). Moreover, Dr. Klibanov agreed that Table 2 from the same text provides guidance to the ordinarily-skilled artisan to help identify "some functional groups that are susceptible to oxidation." (Tr. 524:13-19; 526:1-11.) Thus, there is no dispute that it was possible for a POSA to apply functional group chemistry in order to "anticipate the potential modes of degradation that drug molecules will likely undergo," including oxidative degradation. (SOF 111.) Dr. Klibanov, himself, confirmed the predictive value of structural examination when he opined that a POSA could determine, just on the basis of the type of carbamate functional group present in the molecule (monomethyl vs. dialkyl), whether the molecule would be susceptible to hydrolysis. (Tr. 379:16-380:5; 384:16-385:1.)

Dr. Klibanov further attempted to argue that a POSA could not determine that a drug would be susceptible to oxidation because "the mechanisms of oxidation reactions are usually complex." (Tr. 420:18-421:11.) As Dr. Schöneich explained, Dr. Klibanov's statements that mechanisms of oxidation are complex confuse two concepts. (Tr. 78:6-21.) The first concept is whether a drug like rivastigmine is susceptible to oxidation. This susceptibility is an inherent characteristic of the molecule based on its chemical structure. As Dr. Schöneich demonstrated, the structural features that cause a particular carbon-hydrogen bond in a molecule to be weaker and therefore susceptible to oxidation are predictable and can be looked up in chemistry textbooks. The second concept is the actual reaction mechanism that occurs once the weak carbon-hydrogen bond is broken creating a free radical on the drug. Because radicals are highly reactive, they can react with various components in the formulation including other drug molecules creating a chain reaction. The pathways the free radical reactions may follow are varied and can lead to different reaction products, but they all cause loss of the drug. (SOF 151-52.) Thus, any "complexity" in predicting the variety of mechanistic reaction steps that might occur after radical formation misses the point: what is not complex is the critical determination that the molecule is susceptible to an oxidative pathway in the first instance.

Furthermore, Dr. Klibanov's statements that the oxidation of drugs cannot be predicted because the mechanism is complicated is belied by his own citation to tabulated information in textbooks providing some common functional groups that the POSA would reasonably expect, if present in a molecule, to be subject to oxidation. (Tr. 524:13-19; 524:1-11; PTX 153 at 183.) The predictive value of chemical structure analysis to the POSA is evidenced by such textbooks instructing the artisan to consider a molecule's structural features in helping anticipate likely modes of degradation. To the extent Plaintiffs assert that there is no way to predict whether a

drug in a specific formulation will actually degrade oxidatively without actual testing, Noven responds that the predictive value of chemical structure analysis need only provide the POSA with a reasonable expectation the drug will oxidatively degrade. Absolute certainty is not required. *Warner Chilcott Co., LLC v. Teva Pharms. USA, Inc.*, No. 2014-1439, 2014 U.S. App. LEXIS 21946 at *15-16 (Fed. Cir. Nov. 18, 2014) (affirming summary judgment of invalidity on obviousness where a POSA would have had reasonable expectation of success because "obviousness does not require absolute certainty or a guarantee of success").

(b) It is irrelevant that drugs that a POSA might regard as susceptible to oxidation are ultimately formulated without an antioxidant.

Dr. Klibanov attempts to debunk Dr. Schöneich's substantive analysis by citing to approved pharmaceutical formulations that contain an active ingredient having at least one of the structural features upon which Dr. Schöneich bases his opinion, but do not otherwise list an antioxidant as an ingredient, thus implying that Dr. Schöneich's analysis contains no meaningful predictive value. Rather than address the scientific rationale provided by Dr. Schöneich, Dr. Klibanov stated that Dr. Schöneich's opinions are contradicted by "the experimental data available at the time of the invention involving commercial drugs that were on the market that were FDA approved." (Tr. 317:3-8.) Dr. Klibanov's argument is directly refuted by his own testimony and that of Noven's experts.

Dr. Klibanov did not provide any "experimental data . . . involving commercial drugs," but rather testified about commercial drugs from the Physicians' Desk Reference that did not contain an antioxidant as a listed ingredient. (Tr. 437:10-439:9.) Dr. Klibanov's testimony proves nothing. Dr. Klibanov agreed with Dr. Schöneich that absence of an antioxidant in marketed drug products would not demonstrate to a POSA that the drug is not susceptible to oxidative degradation, thus rendering Dr. Klibanov's comparison to other drugs and their

formulations completely irrelevant. (SOF 168.) Dr. Klibanov further agrees with Dr. Schöneich that the ordinarily-skilled artisan would not conclude that a drug was not susceptible to oxidation because an antioxidant was not used in the formulation because there were other known methods to prevent oxidation of susceptible drugs. (SOF 168 at Tr. 551:23-552:16.) For example, the formulator could address the problem by excluding oxygen, formulating in a dry dosage form, or formulating the drug as a salt. (SOF 168.)

The fact that the five compounds selected by Dr. Klibanov as having a tertiary carbon that is adjacent to both an aromatic ring and an amine (i.e., ampicillin[6], hydroxyzine, meclizine, mirtazapine, and benzquinamide) are marketed in formulations without an antioxidant does not rebut Dr. Schöneich's opinions regarding the susceptibility to oxidation of molecules containing these three features. In fact, each of these marketed examples are formulated in ways known to reduce or eliminate oxidation. Four of the compounds (ampicillin, meclizine, mirtazapine, and benzquinamide) are marketed as dry compositions (SOF 170), which is significant because formulating in a dry state was one known way to reduce or prevent oxidation. (SOF 166 at Tr. 91:8-92:2.) The remaining compound, hydroxyzine, as well as the dry compositions containing meclizine and benzquinamide, are marketed as salts (SOF 170 at Tr. 556:15-557:22; 562:1-10), which is another known way to reduce oxidation. (SOF 166-67.) Further, these marketed compositions may also exploit strategies for minimizing oxidation not listed on the product labeling such as excluding oxygen. (SOF 168.)

The remaining compounds discussed by Dr. Klibanov (dexsecoverine, secoverine, scopolamine, fentanyl, benztropine, physostigmine, and dextromethorphan) do not have the

[6] Dr. Klibanov admitted that unlike rivastigmine, ampicillin has a primary amine and does not have a tertiary amine adjacent to the subject carbon. (Tr. 555:14-19.)

combination of structural features found in rivastigmine that would inform a POSA that the molecule is, like rivastigmine, "particularly susceptible" to oxidation. (SOF 171.)

(c) Dr. Schöneich Considered the Whole Molecule.

Dr. Klibanov's testimony that a POSA must consider the "whole molecule" (Tr. 316:2-317:8) is unavailing because Dr. Schöneich did in fact consider the entire rivastigmine molecule in his presentation to the Court. Dr. Schöneich did not limit his analysis to any part of the rivastigmine molecule. Indeed, he stated that a POSA would have arrived at the conclusion that rivastigmine was susceptible to oxidation by looking at the "structure of the molecule." (Tr. 44:16-22, *see also* 73:17-24; 74:5-8; 74:21-23.) Moreover, Dr. Schöneich explicitly considered the entire rivastigmine molecule discussing: (i) the aromatic ring at the center of the structure (Tr. 48:15-23; 75:13-20), (ii) the "right" side of the structure containing the benzylic carbon and the three substituents bonded to it (Tr. 48:24-49:13; 75:10-23), and (iii) the impact, if any, of the "left" side of the molecule containing a dialkyl carbamate (Tr. 81:7-82:12). Dr. Klibanov offered no testimony that some part of the rivastigmine molecule was overlooked by Dr. Schöneich, nor does Dr. Klibanov provide testimony that that some part of the rivastigmine molecule changes the result or confounds Dr. Schöneich's opinions about rivastigmine.

Dr. Klibanov's reliance on JTX 33 to show that the two tertiary amines in physostigmine facilitate hydrolysis of the carbamate group on the other side of the molecule (Tr. 424:6-425:23) is meaningless here because, as Dr. Klibanov conceded, those features are not present in rivastigmine. (Tr. 520:16-521:11.) Thus, Dr. Klibanov's broad pronouncement that structural features in one area of the molecule can impact properties of the molecule largely ascribed to structural features elsewhere in the molecule is not tied to rivastigmine.

(d) The Inventors' Alleged Experience with Rivastigmine is Irrelevant.

Plaintiffs' attempts to substitute the inventors for persons of ordinary skill in the art fail legally and factually. Because obviousness is based on the hypothetical POSA aware of all the pertinent art, evidence that specific individuals did not combine the prior art is largely irrelevant. *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1364 (Fed. Cir. 2001) (finding that it is "erroneous as a matter of law" to find nonobviousness based on testimony of an expert that he himself had never thought of combining the prior art to arrive at the claimed invention). Indeed, it is erroneous as a matter of law to find nonobviousness based on the skill level of an inventor rather than the hypothetical POSA. *Ebay Inc. v. Kelora Systems, LLC*, No. 10-4947, 2012 WL 1835722 at *10 (N.D. Cal. May 21, 2012) (actual inventor's skill is irrelevant to the obviousness inquiry.) (order).

One of ordinary skill in the art is presumed to know all the pertinent prior art. *Chem. Separation Tech., Inc. v. U.S.*, 51 Fed. Cl. 771, 794 (Fed. Cl. 2002), *aff'd*, 224 Fed. App'x 976 (Fed. Cir. 2007); *In re GPAC, Inc.*, 57 F.3d 1573, 1579 (Fed. Cir. 1995); *In re* Wood, 599 F.2d 1032 (CCPA 1979) (affirming a finding of obviousness where the prior art patent issued 64 years before the asserted patent was filed). There was no evidence that the inventors were aware of the pertinent prior art including Ebert, Elmalem, Sasaki, and the Handbook of Pharmaceutical Excipients. (SOF 10.) One of ordinary skill in this art is required to know, or collaborate with one who knows, organic chemistry. (SOF 1-2.) There is no evidence that the inventors were organic chemists or collaborated with individuals having knowledge of organic chemistry. (SOF 11.) In this case the inventors were blinded by their own experience with rivastigmine tartrate, a salt, which (a) was confidential to Novartis and thus not part of the prior art, and (b) led them

astray when attempting to design a transdermal delivery system containing rivastigmine itself. (*See* Tr. 534:14-535:17.)

(e) The Art Did Not Teach that Rivastigmine Was Stable.

The prior art did not teach that rivastigmine was stable to oxidative degradation. Dr. Klibanov repeatedly stated that the prior art depicts the stability of rivastigmine (or its enantiomer, RA_7) in a "favorable light." (Tr. 359:20-24; 406:4-10.) In each case, however, this "favorable light" is merely that RA_7 is less susceptible to hydrolysis than physostigmine, a compound known to be very susceptible to *hydrolysis*. (*See, e.g.*, Tr. 81:7-82:19; 83:3-84:16; 379:16-380:5; 384:16-385:1; 386:18-387:19.) Dr. Klibanov explained that compounds containing a monomethyl carbamate, like physostigmine, were known to have half-lives as short as 8.5 days. (Tr. 387:1-5.) In other words, when exposed to water, half of the amount of compounds like physostigmine degrades due to hydrolysis in slightly more than a week. (*Id.*) The fact that rivastigmine was less susceptible to hydrolysis than physostigmine, a particularly susceptible compound, says little about the stability of rivastigmine to *free-radical reactions*, such as *oxidation*. (*See, e.g.*, Tr. 444:14-22 (Dr. Klibanov discussing free radicals as causing oxidation).)

That rivastigmine was less susceptible than physostigmine to hydrolysis would not affect a POSA's conclusion that rivastigmine was susceptible to oxidation. Physostigmine does not have a carbon-hydrogen bond at a tertiary carbon that is adjacent to an aromatic group and a tertiary amine as found in rivastigmine. (SOF 171.) Due to the differences in chemical structure, a POSA would not assume that rivastigmine was not susceptible to oxidation just because it was resistant to hydrolysis. (SOF 156.)

B. A POSA Would Have Reasonably Expected that Adding an Antioxidant Would Succeed in Preventing Oxidative Degradation of Rivastigmine.

A POSA would have had a reasonable expectation that adding an antioxidant to a rivastigmine formulation would prevent oxidative degradation of the rivastigmine. (SOF 182-83.) Oxidative degradation was known to be a primary cause of degradation in pharmaceutical compositions, and antioxidants were a well-known and common solution. (SOF 111, 120.) Remington's (JTX 5) explains that "[o]xidation is a prime cause of product instability," and that "[o]xidation may be inhibited by the use of antioxidants, called negative catalysts. They are very effective at stabilizing pharmaceutical products undergoing a free radical mediated chain reaction." (SOF 120.) Remington's and the Handbook of Pharmaceutical Excipients ("Handbook") indicate that all of the antioxidants listed in claim 16 are commonly-used antioxidants. (SOF 96, 121.) And the evidence at trial confirms the conventionality and safe use of the antioxidants specifically recited in claim 16 of the '031 patent. Ansel (DTX 91) lists BHA, BHT, sodium metabisulfite, and propyl gallate as antioxidants "used to prevent the deterioration of preparations by the oxidative process." (SOF 105.)

The antioxidants recited by claim 16 were well-characterized, and commonly understood to be safe. The Handbook discloses what types of substances are incompatible with each of the antioxidants listed in claim 16. (SOF 94.) Amine-containing compounds like rivastigmine are not identified to be incompatible with tocopherol, BHA, BHT, or propyl gallate. (SOF 94, 99.) Each of the antioxidants listed in claim 16 were included on the FDA's Generally Recognized as Safe (GRAS) list, were included in the FDA's Inactive Ingredients Guide, and were also accepted as a food additive in Europe. (SOF 96) Tocopherol, BHA, BHT, and propyl gallate were included in the FDA's Inactive Ingredients Guide for topical formulations, which encompasses transdermal formulations. (SOF 97.) Several of the antioxidants are, in fact,

vitamins (tocopherol is vitamin E; ascorbic acid is vitamin C). (SOF 98.) Persons of ordinary skill would not be concerned that the addition of such antioxidants would be dangerous. And only one of the antioxidants listed in claim 16 need be obvious for the claim to be invalid. *See Schering Corp. v. Geneva Pharms., Inc.*, 339 F.3d 1373, 1380 (Fed. Cir. 2003) (holding a claim invalid as anticipated when it claimed compounds in Markush form and a prior art reference disclosed one of the claimed compounds); *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 782 (Fed. Cir. 1985) ("It is also an elementary principle of patent law that when, as by a recitation of ranges or otherwise, a claim covers several compositions, the claim is 'anticipated' if one of them is in the prior art.").

Further, the experimental results of which a POSA would have been aware showed that rivastigmine was compatible with at least several different antioxidants. GB 040 discloses rivastigmine in a transdermal formulation with BHA and citric acid,[7] from which a POSA would have concluded that these common antioxidants were compatible with rivastigmine. (SOF 32, 196.) A POSA would have drawn the same conclusion as to the reported combination of rivastigmine with sodium metabisulphite, another common antioxidant. (SOF 46, 101.) Amine-containing compounds like rivastigmine were also taught to be compatible with tocopherol, as compositions containing tocopherol and amine drugs were tested and found to be stable for three months under accelerated (40 °C) conditions. (SOF 81.)

Moreover, Plaintiffs cannot argue that the prior art "taught away" from antioxidant use with rivastigmine. *See Santarus, Inc. v. Par Pharm., Inc.*, 694 F.3d 1344, 1355 (Fed. Cir. 2012) (prior art taught away from the claimed invention where the prior art expressly "ruled out" using

[7] GB 040 discloses, in Example 2, a rivastigmine transdermal composition that includes the ingredient Brij 97. (SOF 31.) A POSA would have known that Brij 97 contained two antioxidants, BHA and citric acid. (SOF 31, 123.)

the technology of the invention). Teaching away requires a showing that adding an antioxidant to a rivastigmine composition "is unlikely to be productive of the result sought by the applicant," a stable composition, and no reference asserted by Plaintiffs states or even suggests this. *See id.* at 1354. Dr. Klibanov overstates the prior art's alleged concern for antioxidants in pharmaceutical products or the compatibility issues they pose. For example, the EMEA Guidelines (PTX 162), do not instruct not to employ antioxidants, but instead merely suggest that antioxidant use should be justified, and teach that a product be tested with and without antioxidants. (Tr. 505:17-506:6; PTX 162 at 2/4.) Dr. Klibanov provided no testimony that a POSA could not run routine stability tests to identify an appropriate antioxidant, and provided no example of any active ingredient that could not be combined with at least one antioxidant, such as one of the many listed in the Handbook. (Tr. 510:2-510:21.) Vague reference to potential "mild" toxicity issues with antioxidants in general (PTX 184 at 2:66) does not change the prevailing wide acceptance and use of antioxidants in pharmaceutical applications, nor the safe use of the claimed antioxidants, including vitamins E and C (tocopherol and ascorbic acid (SOF 98)) with rivastigmine. (*See* SOF 85-86, 95-96.)

Although Plaintiffs may argue that other methods were available to solve oxidative degradation problems, the law requires only that the option of using an antioxidant be a suitable option, not the best or only option. *See L-3 Commc'ns. Corp.*, at *14-15. And to the extent the inventors' own experience is relevant to the obviousness inquiry, there was no evidence at trial that they considered any option other than use of antioxidant in transdermal formulations. (Tr. 612:16-22.)

C. Claims 7 and 16 of the '031 Patent are Invalid as Obvious over the Prior Art.

Based on the reasonable expectation that rivastigmine was susceptible to oxidative degradation, and the reasonable expectation that rivastigmine could be paired with an antioxidant

to prevent such degradation in a pharmaceutical formulation, a POSA would have arrived at the subject matter of claims 7 and 16 of the '031 patent based on the undisputed disclosures in the prior art. The POSA's understanding of the prior art disclosures would have been accompanied by the reasonable expectation that rivastigmine was susceptible to oxidative degradation, as explained above.

1. Claim 7 Is Invalid.

Claim 7 depends from claim 1, and encompasses a transdermal device that comprises (A) a pharmaceutical composition that comprises (i) a therapeutically effective amount of rivastigmine, (ii) about 0.01 to about 0.5 weight percent of an antioxidant, and (iii) a diluent or carrier, and (B) a substrate.[8] (SOF 189.) Claim 7 is not limited to any particular antioxidant. (*Id*.)

UK Patent Application GB 2 203 040 ("GB 040"; JTX 19) indisputably discloses a transdermal device with a substrate that contains a therapeutically effective amount of rivastigmine and a diluent/carrier. (SOF 190-94.) A POSA would have had good reason in January 1998 to prepare a pharmaceutical composition containing rivastigmine and would have been motivated to start with GB 040 because rivastigmine was known to be beneficially therapeutic and suitable for transdermal use with dementia patients. (SOF 12-20, 172.) Plaintiffs offered no evidence to the contrary.

Sasaki (DTX 12), which was not before the examiner during prosecution of the '031 patent, is a Japanese patent application that discloses adding an antioxidant (tocopherol) to a transdermal composition to prevent oxidative degradation of the active drug in that composition. (SOF 71, 74-76, 78-79.) Specifically, Sasaki discloses the addition of tocopherol to prevent

[8] The Court has construed certain claim terms, and the Parties have agreed to the construction of certain terms. Order, D.I. 107; Pretrial Order, D.I. 143 at Ex. 1 at ¶¶ 18-19.

oxidative degradation of amino compounds when blended with an acrylic adhesive. (SOF 72, 74, 76.) Sasaki teaches that an antioxidant works, where other methods, such as using oxygen-impervious packaging, do not. (SOF 75-76, 78.) And it is undisputed that Sasaki discloses an amount of antioxidant, tocopherol, that will prevent oxidation that, when applied to Example 2, is 0.22 to 0.44 weight percent, which falls within the 0.01 to 0.5 weight percentage of antioxidant limitation of claim 7. (SOF 77, 211.)

A POSA would have been motivated to combine GB 040 with the teaching of Sasaki and would have arrived at the subject matter of claim 7 of the '031 patent. (SOF 209-10.) GB 040 teaches, in Example 2, rivastigmine combined with an acrylic adhesive. (SOF 31, 209.) Sasaki teaches that, even when enclosed in transdermal packaging that is impervious to oxygen, an amino compound that is blended with an acrylic adhesive is subject to oxidative degradation. (SOF 74-76, 78.) There is no dispute that rivastigmine is an amino compound. (SOF 72-73.) Therefore, a POSA would have understood from Sasaki that rivastigmine, blended with an acrylic adhesive in example 2 of GB 040, would degrade oxidatively. (SOF 72-73, 78, 208-09.) This is especially true since a POSA would have recognized that the tertiary amine in rivastigmine was susceptible to oxidative degradation. (SOF 147, 158.) Moreover, a POSA would have known that acrylic adhesives, like those in Sasaki, were commonly made by a free radical reaction and were a potential source of free radical initiators that can cause the oxidative degradation of susceptible drugs. (SOF 138.)

Dr. Klibanov's attempts to refute the teachings of Sasaki fail. Dr. Klibanov testified that transdermal compositions containing an active ingredient with an amine were commercially available or patented but did not contain an antioxidant. This testimony has no relevance to the combination GB 040 and Sasaki because Dr. Klibanov failed to address whether these

compositions contain an acrylic adhesive. (Tr. 549:12-550:7.) A POSA, knowing from Sasaki that amine drugs are incompatible with acrylic adhesives and that acrylic adhesives are a source of initiators of oxidation, could have chosen to formulate the amine drugs in a different class of polymer not requiring the use of an antioxidant. (Moreover, as demonstrated in the Watson trial, antioxidants can be present in effective amounts without being among the listed ingredients in a formulation. (Trial Opinion, *Novartis v Watson,* No. 11-1077-RGA (consolidated) at D.I. 40, at 8 (BHT introduced into Watson product by an upstream supplier as an impurity), 9 (BHT is not identified in Watson's ANDA).)

Knowing that rivastigmine was susceptible to oxidative degradation, the disclosures of the Handbook of Pharmaceutical Excipients (JTX 8) would have reinforced the POSA's reasonable expectation that an antioxidant could be paired with rivastigmine, in conventional amounts. (SOF 185, 200.) The Handbook discloses a variety of excipients that can be used in pharmaceutical compositions, and the amount typically employed. (SOF 83-84, 86.) The Handbook is a resource for pharmaceutical scientists during pharmaceutical product development. (*Id*.) While Sasaki suggests the use of a concentration of tocopherol that falls within the concentration range required by claim 7, to solve an oxidation problem, the Handbook further discloses that the commonly-used concentration of BHA and BHT for topical (including transdermal) pharmaceutical applications is 0.005-0.02% and 0.0075-0.1%, respectively. This range overlaps with the weight percentage concentration of about 0.01 to about 0.5 weight percent that is required by claim 7.[9] (SOF 88, 91, 199-201.)

[9] Plaintiffs did not offer any evidence that the amount of antioxidant required by claim 7 (which is not limited to any particular antioxidant) was anything other than the conventional amount, or an amount that the POSA could not have arrived at by anything other than routine optimization.

A POSA would have additionally been motivated to consider GB 040 in combination with Ebert (JTX 28) and would have arrived at the subject matter of claim 7 because the similarity in structure between nicotine and rivastigmine would have led a POSA to seek guidance from the prior art, and in particular prior art that disclosed transdermal devices. (SOF 186, 198, 202.) Ebert, another reference that was not before the examiner during prosecution of the '031 patent, (SOF 7), discloses that nicotine in a transdermal patch composition degrades oxidatively and teaches that the solution to oxidative degradation is the addition of an antioxidant. (SOF 64, 67-68, 203.) Ebert discloses that BHT should be added to nicotine compositions at approximately 0.01-1% weight percentage to prevent oxidation, which overlaps with claim 7's range of about 0.01 to about 0.5 weight percentage of antioxidant. (SOF 68, 188, 199.) Numerous other antioxidants are disclosed to be suitable, including BHA and tocopherol. (SOF 69.)

Plaintiffs may argue that Ebert is not applicable to rivastigmine because it is directed to a specialized manufacturing process applicable to volatile drugs. Plaintiffs are incorrect. A POSA would have been well aware that rivastigmine free base is a volatile liquid. (SOF 108.) In any case, a POSA would have understood that the teachings of Ebert are not limited to stabilization during the manufacturing process. (SOF 70.)

Elmalem (JTX 21), another reference that was not before the examiner of the '031 patent, (SOF 7), would have further informed the POSA that rivastigmine was susceptible to oxidative degradation and should be accompanied by an antioxidant. Elmalem discloses various drugs, including RA_7, in solution with the express disclosure that each was paired with an antioxidant "to prevent oxidation." (SOF 36-37.) Elmalem unambiguously discloses that RA_6, RA_7, RA_{15}, physostigmine, and morphine, as the agents tested, "were made up freshly in sterile saline, which

included an equal weight of sodium metabisulphite, to prevent oxidation." (SOF 36-37.) A POSA would have understood that this teaching with respect to RA_7, the racemate of rivastigmine, (SOF 40-41, 204), applied equally to rivastigmine, because RA_7 and rivastigmine are indisputably equally subject to oxidative degradation.[10] (SOF 41.) The teaching of Elmalem is consistent with a POSA's understanding that rivastigmine, based on its structure, would be susceptible to oxidative degradation. (SOF 158-60.) And because transdermal devices require that the drug remain in solution, a POSA would have deemed Elmalem's disclosure of antioxidant added to an RA_7 solution to be relevant to the transdermal device of GB 040. (SOF 48, 204.) A POSA's understanding of Elmalem is reinforced by Weinstock 1981 (JTX 30), because in that reference, authored by professor Weinstock, lead author of Elmalem, antioxidant was added to only those drugs that required antioxidant. (SOF 51-54.)

The '807 Patent (JTX 17) discloses and claims the compounds RA_6, RA_7, and RA_{15}, and a method of treating dementia and other disorders using these compounds. (SOF 58.) The '807 Patent also reinforces the expectation that RA_7 (and hence rivastigmine) is susceptible to oxidation because it expressly discloses preferred antioxidants for the compounds disclosed therein, (SOF 60), and RA_7 is among several compounds that are expressly disclosed and claimed in the '807 Patent. (SOF 58.) Elmalem is consistent with the '807 Patent, because Elmalem discloses that sodium metabisulphite is the antioxidant that is mixed with RA_6, RA_7, and RA_{15} solutions to prevent oxidation of those drugs, and the '807 Patent discloses sodium metabisulphite as a preferred antioxidant for RA_6, RA_7, and RA_{15} (SOF 36-37, 60). It strains credulity to assert, as Dr. Klibanov has (Tr. 364:11-17), that a POSA would be distracted by the generic disclosure of "millions" of compounds when RA_7 is expressly disclosed and claimed,

[10] GB 040 discloses that RA_7 is a racemic mixture of rivastigmine, which can be easily separated into rivastigmine and its enantiomer. (SOF 23.)

along with only two other compounds (RA_6 and RA_{15}). (SOF 58.) Instead, the teaching of the '807 Patent is consistent with the understanding of a POSA that rivastigmine, based on its structure, would be susceptible to oxidative degradation. (SOF 158-60.) Further, the '807 Patent's disclosure is relevant even if it does not directly mention a transdermal composition because the drug in a transdermal device remains in solution. (SOF 62.)

Accordingly, claim 7 of the '031 patent would have been obvious to a POSA in view of the prior art and the POSA's expectation that rivastigmine is susceptible to oxidative degradation.

2. Claim 16 Is Invalid.

Claim 16, which depends from claim 15, is directed to a method of stabilizing rivastigmine by adding an effective amount of antioxidant, where the antioxidant can be any of those recited: tocopherol, ascorbic acid, BHT, BHA, and propyl gallate. (SOF 215-16.) As set forth above, the POSA in January 1998 would have maintained a reasonable expectation that an antioxidant could be combined with rivastigmine in order to prevent oxidative degradation. (SOF 183.) Furthermore, the specific antioxidants recited in claim 16 were well-known and well-characterized excipients for use in pharmaceutical formulation. (SOF 94, 96, 121.)

A POSA would have been motivated to combine GB 040 with Sasaki and would have arrived at the subject matter of claim 16 for the reasons stated above. (SOF 208-10, 213.) GB 040 discloses a rivastigmine composition that included two antioxidants. (SOF 31, 123, 196-98; *see* n 7, supra).) Sasaki discloses the addition of tocopherol to compositions containing an amino drug, like rivastigmine, to prevent oxidation. (SOF 72-73, 78, 81.) The amount of antioxidant disclosed by Sasaki, 0.22 to 0.44 weight percent, is effective to stabilize rivastigmine. (SOF 77-78, 81, 219.) Tocopherol is one of the antioxidants listed in claim 16. (SOF 215-16.) A POSA would have had a reasonable expectation that the composition resulting from the combination of the teachings of GB 040 and Sasaki would be stable. (SOF 77-78, 81, 219.)

The Handbook (JTX 8) discloses an effective amount of each of the other antioxidants listed in claim 16. (SOF 86-93, 201, 217.) As described above, a POSA would have been motivated to add an antioxidant to the rivastigmine composition of GB 040 by combining the teachings of the Handbook with GB 040 based on the POSA's understanding that rivastigmine was susceptible to oxidation. (SOF 200.)

Ebert (JTX 28), too, discloses the addition of an amount of antioxidant, BHT, that is effective to stabilize a composition containing nicotine, (SOF 68), which, as described above, is a compound that is similar in structure to rivastigmine. (SOF 161, 163.) Ebert further states that several other antioxidants listed in claim 16, in particular BHA and tocopherol, are suitable for use in a nicotine composition. (SOF 69.)

Elmalem (JTX 21) discloses the addition of an effective amount of antioxidant, sodium metabisulphite, added to a composition of rivastigmine. (SOF 37, 54, 205, 220-21.) The solution contains RA_7 (which is half rivastigmine), saline, and an antioxidant. (SOF 38-40.) Elmalem specifically states that the addition of antioxidant is "to prevent oxidation." (SOF 37.) The amount of antioxidant disclosed by Elmalem is two parts of antioxidant to one part of rivastigmine. (SOF 42.) This is a higher ratio of antioxidant to rivastigmine than is disclosed by the '031 patent as being sufficient to prevent degradation. (SOF 221-23.)

If Plaintiffs argue that the amount of antioxidant disclosed by Elmalem in combination with RA_7 is somehow too great an amount, this contradicts the statements made during prosecution of the '031 patent that "Applicants do not surrender embodiments . . . where an infringer uses some excess of antioxidant needed for stabilization." (JTX 3 at N0001078.) The Applicants further stated that claim 16 (then claim 25) had been "amended to recite that the amount of antioxidant present is an amount effective to stabilize Compound A from degradation,

thereby literally embracing an embodiment where an infringer uses *any excess of antioxidant necessary* to provide the stabilization." (*Id*. (emphasis added).) Plaintiffs placed no limit on the amount of antioxidant within a composition for purposes of infringement, and they may not limit the prior art now.

The '807 patent discloses that sodium metabisulphite is a preferred antioxidant for use with RA_7 (which is half rivastigmine), which would have provided a further motivation to use an antioxidant to stabilize the rivastigmine composition of Example 2 of GB 040. (SOF 60, 207.)

Accordingly, claim 16 of the '031 patent would have been obvious to a POSA in view of the prior art and the POSA's expectation that rivastigmine is susceptible to oxidative degradation.

D. Claims 7 and 16 of the '031 Patent Are Invalid for Obviousness-Type Double-Patenting.

The doctrine of obviousness-type double patenting, or nonstatutory double patenting, prevents Novartis AG from extending the statutory right to exclude by obtaining claims in the later-expiring '031 patent that are not patentably distinct from claims in a commonly owned earlier-expiring patent. *See Gilead Sciences, Inc. v. Natco Pharm. Ltd.*, 753 F.3d 1208, 1210 (Fed. Cir. 2013); *In re Hubbell*, 709 F.3d 1140, 1145 (Fed. Cir. 2013); *In re Basell Poliolefine Italia S.P.A.*, 547 F.3d 1371, 1375 (Fed. Cir. 2008). In this case, the '031 patent and the '176 patent are commonly-owned for purposes of the double-patenting analysis because these two patents have a common assignee, Novartis AG. The '031 patent is jointly owned by Novartis AG and LTS. (Pretrial Order Statement of Stipulated Facts, D.I. 143-1, ¶10.) The earlier expiring patent, U.S. Patent No. 5,602,176 (JTX 20; the "'176 patent"), is assigned to Novartis AG. (SOF 227-28.) Given the common assignee, there is no need to show that a POSA would start with the claims of the '176 patent to show a motivation to modify the prior art since it is presumed that the POSA starts with the claims of the earlier patent. *Geneva Pharms., Inc. v.*

GlaxoSmithKline, Inc., 349 F.3d 1373, 1377 n.1 (Fed. Cir. 2003). Instead, the question for the Court is whether the claims of the '031 patent would have been obvious over the claims of the '176 patent read in light of the prior art. *In re Longi*, 759 F.2d 887, 893 (Fed. Cir. 1985); *In re Research Corp. Techs, Inc.*, No. 97-2836, 1999 U.S. Dist. LEXIS 22589 (D.N.J. Oct. 25, 1999).

The obviousness-type double patenting analysis involves two steps: 1) the court construes the claims of the earlier and later patents and determines any differences; and 2) the court determines whether those differences render the claims of the later patent non-obvious over the claims in the earlier patent in light of the prior art. *Abbvie Inc. v. Matilda and Terence Kennedy Inst. of Rheumatology Trust*, 764 F.3d 1366, 1374 (Fed. Cir. 2014); *Eli Lilly v. Barr Labs., Inc.*, 251 F.3d 955, 968 (Fed. Cir. 2001); *In re Longi*, 759 F.2d at 893. Invalidity for nonstatutory double patenting is a question of law. *Abbvie*, 764 F.3d at 1372.

The policies behind obviousness-type double patenting support invalidating Novartis AG's attempt to extend its monopoly, as the doctrine is grounded in the public policy reflected in 35 U.S.C. § 101, which allows an inventor to obtain only one patent for each non-obvious invention. *In re Longi*, 759 F.2d at 892-93. Therefore, the obviousness-type double-patenting analysis applies when the earlier and later patents have a common inventor or a common assignee or owner. *Id.* at 892; *In re Hubbell*, 709 F.3d at 1146 ("double patenting may exist between an issued patent and an application filed by the same inventive entity, or by a different inventive entity having a common inventor, and/or by a common assignee/owner") (internal quotations omitted); *In re Bartfeld*, 925 F.2d 1450, 1451 n. 5 (Fed. Cir. 1991) ("Examiners may 'provisionally reject claims not patentably distinct from the disclosure in a co-pending application having an earlier U.S. filing date and also having either a common assignee or a common inventor.'")

Double patenting is based on a core principle of patent law that an inventor must fully disclose his invention and permit free use of it at the end of its term. *Gilead*, 753 F.3d at 1212. In some situations a patentee can remedy a double patenting rejection by submitting a terminal disclaimer that limits the term of the later patent so that it expires at the same time as the earlier patent, preventing the unjustified extension of the patent term. *Id.* at 1213.

The second policy consideration behind obviousness-type double patenting is the prevention of harassment by multiple assignees. If a patentee assigns the rights to an obvious variant of a reference patent to another party or parties, then the alleged infringer could face harassment by multiple parties over claims that are not patentably distinct. *In re Van Ornum*, 686 F.2d 937, 944-48 (CCPA 1982); *Gilead*, 753 F.3d at 1212-14; *In re Fallaux*, 564 F.3d 1313 (Fed. Cir. 2009); *In re Hubbell*, 709 F.3d 114. Based on this justification, obviousness-type double patenting applies to situations in which a double patenting rejection could not be overcome with a terminal disclaimer. *In re Fallaux*, 564 F.3d at 1319 (justifying an obviousness-type double patenting rejection based on the policy of preventing harassment by multiple assignees where the patentee could not file a terminal disclaimer and "this defect was of the applicant's creation as through assignment it allowed ownership of the applications to be divided among different entities.").

Claims 1, 3, 8, and 11 of the earlier '176 patent render claims 7 and 16 of the '031 patent obvious. (SOF 224.) Claim 1 of the '176 patent provides the molecular structure of rivastigmine. Claim 3 is directed to a composition comprising rivastigmine with a pharmaceutical carrier or diluent. Claim 8 covers a systemic transdermal pharmaceutical composition containing rivastigmine and a carrier suitable for transdermal delivery, and claim 11 recites that the carrier is a transdermal patch. (SOF 230-33.)

All the elements of claim 7 of the ’031 patent are expressly found in the claims of the ’176 patent, except for the substrate element and antioxidant element. (SOF 234.) These differences would have been obvious to a POSA for the reasons set forth above regarding the obviousness of including an antioxidant in the claimed formulation and because it is undisputed that every transdermal device has a substrate. (SOF 235-36.)

All the elements of claim 16 of the ’031 patent are expressly found in the claims of the ’176 patent, except for the antioxidant element. (SOF 238.) This difference would have been obvious to a POSA for the reasons set forth above regarding the obviousness of including an antioxidant in the claimed formulation. (SOF 240.)

Accordingly, claims 7 and 16 of the ’031 patent are invalid for obviousness-type double patenting.

Plaintiffs may argue that the obviousness-type double patenting analysis should not apply to this case because the earlier ’176 and later ’031 patents do not have the same exact ownership. In this case, however, where the ’031 patent is owned by LTS and Novartis AG and the earlier ’176 patent is owned only by Novartis AG, the policy considerations for invalidating the ’031 patent on obviousness-type double patenting grounds still apply. Claims 7 and 16 of the ’031 patent are not patentably distinct from the claims of the ’176 patent, and the common owner of these patents, Novartis AG, has therefore unfairly extended the duration of the ’176 patent term. And Novartis AG does not claim that it has the right to control of the assertion of the ’031 patent. It makes no difference that the ’031 patent is also owned by LTS. If Novartis AG was able to avoid an obviousness-type double patenting rejection by assigning the ’031 patent, not only would Novartis AG’s patent term be unfairly extended, but anyone sued for allegedly infringing the ’031 patent could face multiple harassing lawsuits by the multiple assignees. That there is

not complete overlap of the patent owners does not change the possibility of harassment by multiple lawsuits. The rule would serve no purpose if a common owner could avoid obviousness-type double-patenting by a sham partial assignment to another entity. In addition, whether or not Novartis AG and LTS could have filed a terminal disclaimer to overcome double patenting has no relevance to whether the obviousness-type double patenting analysis applies to this case.

VI. CONCLUSION

For the reasons stated above, claims 7 and 16 of the '031 patent are invalid as obvious and for obviousness-type double patenting.

Respectfully submitted,

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/s/ John C. Phillips, Jr.

John C. Phillips, Jr. (No. 110)
Megan C. Haney (No. 5016)
PHILLIPS, GOLDMAN & SPENCE, P.A.
1200 North Broom Street
Wilmington, DE 19806
(302) 655-4200
jcp@pgslaw.com
mch@pgslaw.com

KENYON & KENYON LLP
Steven J. Lee (*pro hac vice*)
Michael K. Levy (*pro hac vice*)
Christopher J. Coulson (*pro hac vice*)
One Broadway
New York, NY 10004-1007
(212) 425-7200

Attorneys for Defendant
Noven Pharmaceuticals, Inc.